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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/077,817 | 09/14/1998 | DANIEL CAPUT | IVD924 | 6529 |

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SANOFI-SYNTHELABO INC.
9 GREAT VALLEY PARKWAY
P.O. BOX 3026
MALVERN, PA 19355

| EXAMINER | |
|---|---|
| BASI, NIRMAL SINGH | |
| **ART UNIT** | **PAPER NUMBER** |
| 1646 | |

DATE MAILED: 06/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/077,817 | CAPUT ET AL. | |
| | Examiner | Art Unit | |
| | Nirmal S. Basi | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on *29 December 2002*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☐ Claim(s) *5-36,38,44-47,52-73,75-84,86,87 and 89-114* is/are pending in the application.

4a) Of the above claim(s) *5-36,38,52-71 and 89-110* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *44-47, 72-73, 75-84, 86-87, 111-114* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. Amendment filed 12/26/02 has been entered. Applicant has amended claims 72, 78-80, 83, 87 and 111-113. Applicant has cancelled claims 48-51, 74, 85 and 88. Claims 44-47, 72-73, 75-84, 86-87 and 111-114 as they pertain to the elected polypeptide of Group I (polypeptide of SEQ ID NO:2) will be examined. Claims 5-36, 38, 52-71, 89-110, were previously withdrawn from consideration as being directed to a non-elected invention.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action (7/18/00, paper number 1).

3. The proposed drawing correction and/or the proposed substitute sheets of drawings, filed on 4/10/02 were approved by the Examiner in The Office Action dated 7/2/02 (paper number 28). New corrected drawings are required in this application because corrected formal drawings have not been submitted. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

### Claim Rejection, 35 U.S.C. 112

4. Claims 72-73,75-84, 86-87 and 111-114 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 72, 83, 87 remain indefinite because it is not clear what specific regions of the protein comprise a "biologically active fragment" and what activity is contained in said fragment so as to allow the metes and bounds of the claim to be determined. Applicant has not traversed Examiner's rejection as it pertains to a "biologically active fragment".

Claims 78 and 111 remain indefinite because the phrases "stringent conditions" and "allelic variant" are not clearly defined so as to allow the metes and bounds of the claim be determined. Applicant argues one skilled in the art would readily understand the term "allelic variant" and "stringent conditions". Applicant further argues "allelic variant" is recognized and accepted by the PTO as evidenced by issuance of U.S. Patents 5,710,023 and 6,268,480, which use the term. Also argued is that the term "allelic variant" would mean a naturally occurring variant of the nucleotide sequence encoding the IL-13 receptor. Applicant also argues "stringent conditions", as explained in the specification, are those customarily employed by those of skill in the art. Applicant's arguments have been fully considered but are not found persuasive. The term "variant" carries no weight in terms of structure and function and encompasses an unlimited number of alterations and reads on unrelated molecules. Also it is impossible to determine if a particular variant occurs in nature without the knowledge of every sequence of every polypeptide found naturally. Further, if a nucleic acid molecule is mutated and stably expressed in a cell line, does it encode a protein that is naturally occurring? Further "stringent conditions" of hybridization are not specified. The metes and bounds of the group of sequences that would meet the limitations of the claim

depend upon the precise conditions under which hybridizations were performed including wash conditions. Since the hybridization and wash conditions dictate, which nucleic acid sequences remain specifically bound to the nucleic acid the metes and bounds of the claims cannot be determined without the disclosure of said conditions. Further, applicants' reference to issued Patents to overcome the rejection under 35 U.S.C. 112, second paragraph, for the claimed protein, is not persuasive because each application is examined on its own merits. In the decision of *In re Hutchison*, 69 USPQ 138 (CCPA, 1946), the court held that

> "We are not concerned, of course, with the allowed claims in either the patent or in this application. The sole question for our determination is whether the six article claims on appeal were properly rejected below, and this we pass upon without further reference to, and without comparing them with, the claims in the patent or the claims, which stand allowed in this application."

In essence, the position in the instant application that each application is examined on its own merits can be found in the judicial precedent cited above. The rejections in the instant application will only be withdrawn if they are shown to be legally or factually unsound.

Claim 87 remains indefinite because it is not clear what is the "mature sequence of IL-13 receptor chain protein, IL-13R$\beta$" the "extracellular domain of sequence (a)"or "intracytoplasmic domain of sequence (a)". Further it is not clear what is sequence (a). It is also not clear what fragments (a) –(c) are to referring to. Claim 87 is an independent claim and does not contain subsections (a), (b) and (c). It appears Applicant may have intended to be make claim 87 dependent on claim 83, if that is the case an appropriate amendment must be made. If the claim is an independent claim,

then for clarity, subsections (e)-(h) should be changed to subsection (a)-(d). Applicant argues the terms "mature sequence" is defined in the specification. Applicant also argues the terms "extracellular " and "intracytoplasmic" domain are defined in the specification. Applicant's arguments have been fully considered and are not found persuasive. The claims do not disclose the SEQ ID NO:. The regions of the protein that comprise "mature sequence of IL-13Rβ ", "extracellular domain of sequence (a)" or intracellular domain are disclosed are also not disclosed so as to allow the metes and bounds of the claim to be determined. Further the name IL-13Rβ is not an art accepted term and carries no weight in terms of structure so as to allow the metes and bounds of the claim to be determined. To overcome the rejection, it is suggested, IL-13Rβ be referred to by SEQ ID NO: and the domains be identified by a specific amino acid sequence.

Claims 73, 75-77, 79-82, 84, 86, and 112-114 are indefinite because they depend on an indefinite base claim.

5. Claims 44, 46-47, 72-73, 75-78, 81, 83-84, 86-87,111-114 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the following compounds: a) protein comprising the amino acid of SEQ ID NO:2, b) specific fragments of the protein of SEQ ID NO:2 (e.g. the fragment consisting of residues 1 to 337 of SEQ ID NO:2) which can inhibit the binding of IL-13 to the protein of SEQ ID NO:2, and c) specific fragments of the protein of SEQ ID NO:2 which are of sufficient length to be used as epitopic portions of the polypeptide of SEQ ID NO:2,

wherein said epitopic portions are useful for producing antibodies which bind to the protein of SEQ ID NO:2, does not reasonably provide enablement for other compounds not disclosed in subsections a)-c) above. The, specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant argues claims 72-73, 75-78, 81, 83-84, 86-87 are directed to specifically defined fragments of SEQ ID NO:2, biologically active fragments or allelic variants thereof. Applicant argues the fragment of amino acid residues 1-337 of SEQ ID NO:2 can be used to show inhibition of IL-13 binding. Applicant also argues one skilled in the art would readily understand the term "allelic variant" and "stringent conditions". Applicant further argues "allelic variant" is recognized and accepted by the PTO as evidenced by issuance of U.S. Patents 5,710,023 and 6,268,480, which use the term. Also argued is that the term "allelic variant" would mean a naturally occurring variant of the nucleotide sequence encoding the IL-13 receptor. Applicant also argues "stringent conditions", as explained in the specification, are those customarily employed by those of skill in the art. Also Applicant argues "biological activity" is clearly defined.

Applicant's arguments have been fully considered but are not found persuasive. The term "variant" carries no weight in terms of structure and function and encompasses an unlimited number of alterations and reads on unrelated molecules. Also it is impossible to determine if a particular variant occurs in nature without the knowledge of every sequence of every polypeptide found naturally. Further, if a nucleic acid molecule is mutated and stably expressed in a cell line, does it encode a protein

that is naturally occurring? Further "stringent conditions" of hybridization are not specified and biological activity not clearly define. The scope of the claims depend upon the precise conditions under which hybridizations were performed including wash conditions. The hybridization and wash conditions dictate, which nucleic acid sequences remain specifically bound to the nucleic. Further, applicants' reference to issued Patents as establishing enablement for the claimed protein is not persuasive because each application is examined on its own merits. In the decision of *In re Hutchison*, 69 USPQ 138 (CCPA, 1946), the court held that

> "We are not concerned, of course, with the allowed claims in either the patent or in this application. The sole question for our determination is whether the six article claims on appeal were properly rejected below, and this we pass upon without further reference to, and without comparing them with, the claims in the patent or the claims, which stand allowed in this application."

In essence, the position in the instant application that each application is examined on its own merits can be found in the judicial precedent cited above. The rejections in the instant application will only be withdrawn if they are shown to be legally or factually unsound.

The claims are drawn to isolated protein that binds interleukin-13 or fragments thereof. The specification discloses the protein of SEQ ID NO:2 binds IL-13. The specification also discloses the fragment of amino acid residues 1-337 of SEQ ID NO:2 can be used to show inhibition of IL-13 binding to the protein of SEQ ID NO:2. The critical feature of the isolated protein is that it binds IL-13, said critical feature is contained in a specific sequence of SEQ ID NO:2. Although, it may be argued that since the fragment of amino acid residues 1-337 of SEQ ID NO:2 can be used to show

inhibition of IL-13 binding to the protein of SEQ ID NO:2, said fragment also binds IL-13. This is not necessarily the case. The fragment could reduce binding by interacting directly with the protein of SEQ ID NO:2, thereby causing a conformational change that reduces the binding of IL-13 to said protein. Alternatively, the fragment may reduce the binding of IL-13 to the protein of SEQ ID NO:2 by indirect means. For example, the fragment may have effects on other proteins on the cell surface that may be required for functionality of the protein of SEQ ID NO:2. The direct binding of IL-13 to a fragment of the protein of SEQ ID NO:2 is not disclosed. The structure of SEQ ID NO:2 required for Il-13 binding has not been disclosed. The scope of the claims encompasses other fragments that have not been specifically disclosed to have the critical feature of the invention, and further lack the elements that have been disclosed as enabling. The specification does not identify any minimum size of fragment of SEQ ID NO:2 that would retain activity. Fragments, as written, embrace polypeptides, which may be unrelated to the protein of SEQ ID NO:2. Without disclosure of where specially, in the structure of the molecule, the critical feature is contained, it accordingly follows that the specification does not adequately teach how to make or use a commensurate number of such species. One cannot make or use that which cannot be envisioned. Further the product by process claims may produce protein completely unrelated to the receptor of SEQ ID NO:2. Nucleic acids, not encoding the critical feature of the receptor of SEQ ID NO:2, are also produced using the method as claimed. For example, hybridization conditions may lead to isolation of nucleic acids which encode polypeptides unrelated to the protein of SEQ ID NO: 2. Applicant has not disclosed how to use said

protein/fragments. Many said protein variants may be inactive. Applicant has not disclosed how to use said inactive variants. Applicant has not disclosed the gene encoding claimed protein or allelic variants. The disclosure does not teach how to produce active variants, or to use the numerous fragments which did not share one of the enabled functions set forth above e.g. for the production of an epitope fragment of protein of SEQ. ID. NO:2. Due to the large quantity of experimentation necessary to identify the DNA of instant invention containing the critical feature of the invention, the lack of direction/guidance presented in the specification regarding the identification, purification, isolation and characterization of said DNA, the unpredictability of the effects of mutation on the structure and function of proteins, and the breadth of the claim which fail to recite sufficient structural limitations encompassing the critical feature of the invention, undue experimentation would be required of the skilled artisan to make or use the claimed invention in its full scope.

Further pertaining to claims 78, 87 and 111, the instant fact pattern closely resembles that in Ex parte Maizel, 27 USPQ2d 1662 (BPAI 1992). In Ex parte Maizel, the claimed invention was directed to compounds, which were defined in terms of function rather than sequence (i.e., "biologically functional equivalents"). The only disclosed compound in both the instant case and in Ex parte Maizel was the full length, naturally occurring protein. The Board found that there was no reasonable correlation between the scope of exclusive right desired by Appellant and the scope of enablement set forth in the patent application. Even though Appellant in Ex parte Maizel urged that the biologically functional equivalents would consist of proteins having amino acid

substitutions wherein the substituted amino acids have similar hydrophobicity and charge characteristics such that the substitutions are "conservative" and do not modify the basic functional equivalents of the protein, the Board found that the specification did not support such a definition, and that the claims encompassed an unduly broad number of compounds. Such is the instant situation. Clearly, a single disclosed sequence does not support claims to any protein derived from the same, given the lack of guidance regarding the structure of the nucleotide sequence encoding an interleukin-13 binding polypeptide.

6. Claims 44, 47, 72-73, 75-78, 81, 83-87, 111-114 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed.

Applicant has not traversed Examiners' rejection.

The claims are drawn to isolated polypeptide comprising fragments of SEQ ID NO:2, polypeptide encoded by nucleotide sequences that hybridize to the nucleotide encoding the protein of SEQ ID NO:2, allelic variants.

The neither disclosure, nor prior art provide any data or suggest which fragments of SEQ ID NO:2 have a specific biological activity. The disclosure of the distinct polypeptide of SEQ ID NO:2 (380 amino acids) does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length, truncated, fusion polypeptides and variants thereof; and pharmaceutical compositions comprising said polypeptides. A description of a genus of polypeptides

may be achieved by means of a recitation of a representative number of polypeptides, defined by an amino acid sequence, falling within the scope of the genus or of a recitation of structural and functional features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polypeptides. There is no description of the conserved regions, which are critical to the structure and function of the genus claimed or which sequences may be biologically active and what is that biological activity. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polypeptides encompassed and predict their use. Further no identifying characteristic or property of the instant polypeptides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

The specification further fails to identify and describe the regulatory regions essential to the function of the claimed invention, which are required since the claimed invention currently encompasses the full length, truncated, fusion polypeptides and variants thereof. Since the disclosure fails to describe the common attributes or

characteristics that identify members of the genus, the disclosure of the ability to have any biological active sequence derived from SEQ ID NO:2, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed. The allelic variants are not disclosed. The amino acids that comprise the specific domains is not disclosed.

An adequate written description of a protein, requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention. Accordingly, an adequate written description of a protein is more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the protein itself. Accordingly, the specification does not provide a written description of the scope claimed. Protein comprising specific fragments disclosed to bind interleukin 13 are enabled.

No claim is allowed

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal S. Basi whose telephone number is 571-272-0868. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Nirmal S. Basi
Art Unit 1646
June 9, 2004.

Gary d. Kunz
GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600